

IN THE CLAIMS:

Summary of Current Amendments:

Please cancel Claims 28-47, without prejudice to or disclaimer of the subject matter therein.

Please amend Claims 1, 2 and 4, without prejudice to or disclaimer of the subject matter therein. Claims 3 and 5-27 are reiterated below without amendment.

Listing of Claims:

1. (Currently Amended) A method of structure-based identification of candidate compounds ~~which potentially bind~~ for binding to complement receptor type 2 (CR2) proteins or to a complex of CR2 and its ligand, comprising:

a. providing a three dimensional structure of a CR2 short consensus repeat (SCR) 1-2 region selected from the group consisting of:

i. a structure defined by atomic coordinates of a three dimensional structure of a crystalline CR2 SCR1-2 region in complex with C3d;

ii. a structure defined by atomic coordinates selected from the group consisting of:

(1) atomic coordinates represented in a table selected from the group consisting of Table 2 (CR2-C3d) and Table 3 (CR2 only); and,

(2) atomic coordinates that define a three dimensional structure, wherein at least 50% of said structure has an average root-mean-square deviation (RMSD) from backbone atoms in secondary structure elements in at least one domain of a three dimensional structure represented by said atomic coordinates of (1) of equal to or less than about 1.0 Å; and

iii. a structure defined by atomic coordinates derived from CR2 protein molecules arranged in a crystalline manner in a space group R32 so as to form a unit cell of dimensions $a=b=170.5\text{ Å}$, $c=173.8\text{ Å}$; and,

- b. identifying a candidate compound for binding to said CR2 SCR 1-2 region by performing structure based drug design with said structure of (a).
2. (Currently Amended) The method of Claim 1, wherein said step of identifying comprises selecting candidate compounds that ~~potentially~~ bind to and activate CR2.
3. (Original) The method of Claim 1, wherein said method further comprises:
- c. selecting candidate compounds of (b) that inhibit the binding of CR2 to its ligand.
4. (Currently Amended) The method of Claim 3, wherein said step (c) of selecting comprises:
- i. producing said candidate compound identified in step (b);
- ii. contacting said candidate compound identified in step (b) with CR2 or a fragment thereof and a CR2 ligand or a fragment thereof under conditions in which a CR2-CR2 ligand complex can form in the absence of said candidate compound; and
- iii. measuring the binding affinity of said CR2 or fragment thereof to said CR2 ligand or fragment thereof; wherein a candidate inhibitor compound is selected as a compound that inhibits the binding of CR2 to its ligand when there is a decrease in the binding affinity of said CR2 or fragment thereof for said CR2 ligand or fragment thereof, as compared to in the absence of said candidate inhibitor compound.
5. (Original) The method of Claim 3, wherein said ligand is selected from the group consisting of C3d, CD23, and Epstein Barr Virus (EBV) gp350/220, or CR2-binding fragments thereof.
6. (Original) The method of Claim 3, wherein said ligand is a gp350/220 viral membrane protein from EBV or a CR2-binding fragment thereof.
7. (Original) The method of Claim 3, wherein said CR2 protein or fragment thereof comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.
8. (Original) The method of Claim 1, wherein said method further comprises:

- c. selecting candidate compounds that stabilizes a complex of CR2 with its ligand.
- 9. (Original) The method of Claim 8, wherein step (c) of selecting comprises:
 - i. contacting said candidate compound identified in step (b) with a CR2-CR2 ligand complex, wherein said CR2-CR2 ligand complex comprises CR2 or a fragment thereof and a CR2 ligand, or a fragment thereof;
 - ii. measuring the stability of said CR2-CR2 ligand complex of (i), wherein a candidate stabilizer compound is selected as a compound that stabilizes the CR2-CR2 ligand complex when there is an increase in the stability of the said complex as compared to in the absence of said candidate stabilizer compound.
 - 10. (Original) The method of Claim 8, wherein said ligand is selected from the group consisting of C3d and CD23.
 - 11. (Original) The method of Claim 8, wherein said CR2 protein or fragment thereof comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.
 - 12. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the SCR2 domain of said CR2.
 - 13. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the interface between the SCR1 and SCR2 domains of CR2.
 - 14. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the dimer interface between two CR2 proteins
 - 15. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the interface between CR2 and C3d, C3, a CR2-binding fragment of C3 containing C3d, or a fragment thereof.

16. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the B strand and the B-C loop of CR2 SCR2 comprising the segment: G79-G80-Y81-K82-I83-R84-G85-S86-T87-P88-Y89.

17. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to a site on the B strand of CR2 SCR2 comprising position K100.

18. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to a segment of CR2 SCR2 comprising V130-F131-P132-L133.

19. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to a segment of CR2 SCR2 comprising the fragment T101-N102-F103.

20. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the loop between helix 2-3 of C3d comprising the segment Q68-P69-S70-S71.

21. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to Helix 5 of C3d comprising the segment S104-Q105-V106-L107-C108-G109-A110-V111-K112-W113-L114-I115-L116-E117-K118-Q119-K120-P121-D122.

22. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to Helix 7 of C3d comprising the segment N170-S171-L172-P173-G174-S175-I176-T177-K178-A179-G180-D181-F182-L183-E184-A185.

23. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to amino acid residues at positions 84 and 86 of an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.

24. (Original) The method of Claim 1, wherein said step of identifying comprises directed drug design.

25. (Original) The method of Claim 1, wherein said step of identifying comprises random drug design.

26. (Original) The method of Claim 1, wherein said step of identifying comprises grid-based drug design.

27. (Original) The method of Claim 1, wherein said step of identifying comprises computational screening of one or more databases of chemical compounds.

28-47. (Cancelled)